REMARKS

Reconsideration is respectfully requested. Claims 1- 29 and 31-37 are pending. Claims 1, 2, 19, 35, and 36 have been amended. Claim 30 has been canceled. Claims 14-18 have been withdrawn. No new matter has been added by the amendments. Amendments to the claims do not affect inventorship.

Applicant has not dedicated nor abandoned any unclaimed subject matter. Moreover, Applicant has not acquiesced to any rejections or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Request for Examiner Interview

Applicant respectfully request an Examiner interview before the next Office Action, should the claims not be in condition for allowance.

Claim Amendments

Claims 1, and 19 have been amended for technical clarity. Claims 35 and 36 have been amended to correct dependency.

Claim 2 has been amended. The support for "rules of thermodynamic principles" and "a test for violation of physical and chemical laws" is found, for example, in paragraph [069]:

> In general, the fitness function may consist of several parts.... These "rules" are generally drawn from the literature or thermodynamic principles. ... In another embodiment, the fitness function may include user-definable limiting assumptions, such as a test for multiplicity of steady-states or violation of physical and chemical laws.... In a preferred embodiment the fitness function includes more than one or all of the above described embodiments.

Claim Objections

Claims 35 and 36 are objected to because they depend from a cancelled claim. These claims have been amended to correct their dependencies. As such, Applicant respectfully requests the amendments be entered and the objections be withdrawn.

Claim Rejection under 35 U.S.C. § 101

Claims 19 and 35-37 stand rejected under 35 U.S.C. § 101 on the basis that the claimed invention is directed to non-statutory subject matter. This set of claims contain one independent claim, namely claim 19. As shown below, the amended claims are indeed patentable under 35 U.S.C. § 101.

Claim 19

The Examiners states that:

> The claims do not actually recite a physical transformation of matter or concrete, tangible and useful result. While instant claim 19 recites a memory communicates with a central processing unit, this communication is not a concrete, tangible, AND useful result. The communication can be interpreted to take place solely within the confine of the computer without any communication to the user.

The Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility (1300 OGN 142, November 22, 2005) states:

> [A] practical application of a 35 U.S.C. Sec 101 judicial exception is claimed if the claimed invention physically transforms an article or physical object to a different state or thing, or if the claimed invention otherwise produces a useful, concrete, and tangible result.

Assuming *arguendo* that the claimed invention does not transform an article or physical object to a different state or thing, the invention of claim 19 still produces a useful, concrete, and tangible result. Claim 19, as amended, is directed to a computer for deriving and optimizing a mathematical model for a system. The system includes a central processing unit and a memory that communicates with the central processing unit. The memory contains various modules for deriving and optimizing a hypothetical model of multiple unit operations that each mathematically represent one or more physical, chemical, or biological actions that can be performed on one or more components of the system. The memory also includes a communication module that communicates the hypothetical model that best represents the empirical data to a user in a tangible form.

Providing the hypothetical model that best represents the empirical data to a user is extremely useful. For example, the user can use the optimized model for prediction purposes, such as predicting the weather, which as the Examiner appreciates, is useful. See paragraphs [020] and [132]. As such, amended claim one is directed to statutory subject matter, as the claimed computer produces a useful result that is both concrete and tangible as it is communicated "to a user." In light of the amendments to claim 19, Applicant respectfully requests this rejection be withdrawn.

Claims 35-37

Claims 35-37 are rejected on the basis for failing to result in a physical transformation or recite a concrete, tangible, and useful result. These claims have been amended to correctly depend from claim 1, which the Examiner has not rejected under 35 U.S.C. § 101. A such, Applicant respectfully requests that the rejection be withdrawn as moot.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1 and 2 (and claims 3-13, 20-29, and 31-37 dependent therefrom) stand rejected under 35 U.S.C. § 112, first paragraph, for containing new matter.

MPEP § 2163.02 states:

> Whenever the [new matter] issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed.

The Examiner has rejected claim 2 for the recitation of "ii) a feasibility test against theoretical constraints of thermodynamic principles; and iii) a feasibility test against theoretical constraints of physical laws."

Claim 2 has been amended to recite: "ii) rules of thermodynamic principles; and iii) a test for violation of physical and chemical laws." Support for these amendments can be found, for example, in paragraph [0069] of the present application. As such, Applicant respectfully submits these amendments obviate the rejection.

The Examiner rejects claim 1 for the recitation "communicating said first or second hypothetical model that best represents the system to a user."

The specification discloses in paragraph [024]:

> In some cases, a solution is found (there is convergence on a single solution), which then can be tested experimentally; alternatively, the process does not result in convergence, but several models either equally or closely fit the data, which are then tested; similarly, the process can be used iteratively to generate new models for testing.

The specification further discloses in paragraph [081]:

> In a preferred embodiment, the models are experimentally validated. That is, a model identified either as the global solution or a possible solution can be validated by any number of experimental techniques. In a preferred embodiment one or more of the same parameters are adjusted in competing models "in silico" until competing models predict measureably different outcomes. The same parameter (s) are adjusted in vivo, such as with genetic engineering or metabolic engineering techniques generally known to the art, with the resulting outcome measured and added to the empirical data set. (Emphasis added).

Thus, to test and validate models experimentally, the same parameters of models are adjusted both within a computer (*in silico*) and outside of a computer but inside a cell (*in vivo*). A skilled artisan would appreciate that an *in vivo* experiment is conducted by a human being (e.g., a biologist). To adjust the parameters of models in an *in vivo* experiment, the biologist needs to know what are the parameters. To know what the parameters are, the biologist needs to obtain the parameters from the computer in a form intelligible to the biologist, such by displaying parameters on a screen or printing them out on a piece of paper. As such the model that best represents the system is communicated to a user.

Applicants further draws the Examiner's attention to MPEP §2163.02, which states:

> The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement.

Thus, even if the recitation "communicating said first or second hypothetical model that best represents the system to a user" is not described literally, the application still provides disclosure to satisfy the description requirement, as there is no way a user could use the selected hypothetical model if it was not communicated to the user, such as via a computer display or printout.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claim 19 is rejected as failing to comply with the enablement requirement. The Examiner states that:

> Claim 19 is directed to a computer readable medium that contains unit operations . . . A computer medium . . . is not capable of receiving data and performing operations. A computer may comprise INSTRUCTIONS or a PROGRAM for doing so, but this is not what is claimed.

Claim 19 has been amended to address the Examiners concerns.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-13, 19-29, and 31-37 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 1 is rejected for insufficient antecedent basis for the limitation "said unit operation" on the alleged basis that: "[w]hile there is previous mention of plural 'unit operations', there is no previous mention of a single unit operation." Claim 1 has been amended to recite "providing a plurality of unit operations stored in a computer that each mathematically represent one or more physical, chemical, or biological actions that can be performed on one or more components of a system."

Claim 19 is rejected because of insufficient antecedent basis for the limitation "said memory." Claim 19 has been amended to delete the limitation "said memory." The Examiner also states claim 19 "recites a computer readable medium comprising various modules that are vague and indefinite. It is unclear what Applicant intends the modules to mean. Are they part of a program of some structural feature?" Furthermore, the Examiner states that: "Claim 19 ... recites a computer readable medium comprising various modules.... It is unclear what Applicant intend the modules to mean." Claim 19 has been amended to clarify that the modules are software modules contained within the memory of a computer.

Finally, Claims 35-37 are rejected as vague and indefinite because they depend from a canceled claim. Claims 35-37 have been amended to depend from claim 29.

In light of the above, it is respectfully submitted that all 35 U.S.C. § 112 rejections have been addressed.

Claim Rejection Under 35 U.S.C. § 102

Claims 1-7, 19-22, 27, and 29 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Laurikkala et al. *Computer Meths. Prog. Biomed.* 55:217-228 (1998) ("*Laurikkala*"). Applicant respectfully traverses.

For an anticipation rejection under 35 U.S.C. § 102 to be proper, a single reference must disclose each and every element of a claim. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); M.P.E.P. § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

The present invention is directed to methods and systems to derive and/or optimize a mathematical model of a system comprising unit operations. Each unit operations mathematically represents one or more physical, chemical, or biological actions that can be performed on one or more components of the system.

In contrast, *Laurikkala* discloses a rules-based system driven by empirical measurements. It does not discloses "unit operations" which are "actions that can be performed on one or more components of a system" and a "model comprising a subset of said unit operations," as required by the pending claims.

The Examiner states that:

> It is noted that Laurikkala et al. discloses using an algorithm that modifies an initial population of chromosomes with selection, crossover, and mutation operators including bit values and choosing the most fit chromosomes with a higher probability ... which represents the unit operation as well unit operation as a mathematical representation of a biological process.

Applicant submits that although *Laurikkala* uses the terms "chromosome" and "gene," these terms, as they are used in the present specification, are not mathematical representations of any biological process. *Laurikkala* discloses at page 218, left column:

> A simple genetic algorithm modifies a population consisting of chromosomes (individuals) with selection, crossover and mutation operators. Chromosomes are usually binary strings in which a bit in a fixed position corresponds to a gene, where the value of a bit is equivalent to the allele of a gene.

Nevertheless, when describing the "Galactica" system the terms "chromosome" and "gene" are used for the convenience of describing a mathematical approach (genetic algorithm) that simulates a biological process. For example, *Laurikkala* discloses that: "[r]ule-based concepts are represented with the Pittsburgh style chromosomes." Page 220, right column, third full paragraph. Thus, "[r]ules are coded to sub-symbolic binary strings so that each condition as many bits as the corresponding variable has domain value are reserved." Page 221, left column, second full paragraph. As such, the "chromosomes" disclosed in *Laurikkala* are binary strings representing a collection of rules, and each "gene" of the "chromosome" is a subset of the binary string that may represent a particular decision or condition part of the rules. Therefore, the terms "chromosome" and "gene" are not used to represent a biological process.

Further, it is unclear what in *Laurikkala* is considered by the Examiner to be claimed "unit operations" - the "chromosome", the "gene" , or the "genetic operators" such as "cross-over and mutation operators" disclosed in page 220, left column, second full paragraph.

Because *Laurikkala* does not teach each and every limitation of claim 1 and 19, it cannot not anticipate claims 1 and 19 and claims depend therefrom. As such, it is respectfully requested that this rejection be withdrawn.

Claim Rejection Under 35 U.S.C. § 103

Claims 8, 11-13, 19-29, 31-32, and 34-35 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Laurikkala* in view of Addison (US 2004/0143725 A1) ("*Addison*"). Applicant respectfully traverses.

Claims 9-10, and 36-37 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Laurikkala* in view of *Addison* and further in view of Hood et al. (US 2002/0095259 A1) ("*Hood*"). Applicant respectfully traverses.

Claims 33 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Laurikkala* in view of *Addison* and further in view of Cubicciotti (US 2002/0034757 A1) ("*Cubicciotti*"). Applicant respectfully traverses.

1) The *Graham* Factors

When rejecting claims under 35 U.S.C. §103, the Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. MPEP § 2142. The inquiry of obviousness is controlled by the *Grahm* factors. See *KSR International Co. v. Teleflex Inc.* 1727 S.C.t (2007) (citing *Graham v. John Deere Co. of* Kansas *City*, 383 U.S. 1 (1966)). These factors are: 1) the scope and content of the prior art; 2) the differences between the prior art and the claims; 3) the level of ordinary skill in the pertinent art; and 4) objective evidence of nonobviousness.

As discussed above, *Laurikkala* discloses a rules-based systems driven by empirical measurements. It does not discloses "unit operations" which are "actions that can be performed on one or more system components of a system" and a "model comprising a subset of said unit operations," as the pending claims required." This defect is not cured by *Addison*, *Hood, or Cubicciotti.*

Addison is directed to a computer architecture called Whole Cell Compute, which is based on the biochemical processing of cells. See Abstract. As shown above, it does not teach "unit operations."

Hood is directed to a method of determining a comparative expression profile in an individual by comparing the expression level of a sample of molecules in different populations. See Abstract. Nowhere does it teach anything comparable to "unit operations."

Cubicciotti is directed to single-molecule selection methods for identifying target-binding molecules. See Abstract. It too does not teach "unit operations."

2) There is no reason to combine *Laurikkal* with *Addison* to reach the claimed invention.

"[A] patent composed of several elements is not proved obviousness merely by demonstrating that each of its elements was, independently, known in the prior art.... [I]t can be important to identify a **reason** that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR*, at 1743. Emphasis added.

As discussed above, *Laurikkala* discloses a rules-based systems driven by empirical measurements, *Addison* is directed to a computer architecture called Whole Cell Compute, which is based on the biochemical processing of cells, *Hood* is directed to a method of determining a comparative expression profile in an individual by comparing the expression level of a sample of molecules in different populations, and *Cubicciotti* is directed to single-molecule selection methods for identifying target-binding molecules. None of these references relate to "unit operations," or methods and systems to derive and/or optimize a mathematical model of a system comprising unit operations. Thus there is no apparent reason to combine these references to reach the claimed invention.

The Examiner alleges that the reason to combine the *Laurikkal* with *Addison* is to

> avoid the laborious knowledge acquisition needed for human experts in experts systems by employing machine learning techniques that learn required knowledge automatically, as stated by Laurikkala et al. Page 13 of the instant office action.

Thus motivation to combine *Laurikkal* with *Addison* hinges on the premise that (i) *Addison* is directed to "experts systems", (ii) such system needs "human experts" to acquire knowledge laborious, and (iii) *Laurikkal* provides the "machine learning techniques" so that the "experts systems" can acquire "knowledge automatically."

It is known in the art that an "expert system", also known as a knowledge based system, is a computer program that contains the knowledge and analytical skills of one or more human experts, related to a specific subject. However, as the Examiner states on page 12 of the instant office action:

> Addison describes optimizing techniques and genetic programming techniques for mimicking the behavior of biological cells in complex systems via simulation and mathematical modeling using artificial intelligence.

Thus the system described in *Addison* is a model "for mimicking the behavior of biological cells in complex systems," which is not an "expert system" as known a skilled artisan.

Because *Addison* is not related to an "expert system", there is not motivation to combine it with *Laurikkal* which is directed to "expert system" to provide the "machine learning techniques" so that the *Addison* systems can acquire "knowledge automatically."

For the forgoing reasons the references in combination do not teach each and every limitation of the claimed invention, and there is no plausible reason to combine these references to reach the claimed invention. Accordingly, the Examiner fails to make a *prima facie* case of obviousness and the rejections should be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 442-1000.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

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By: ______________________
Tao Huang, Reg. No. 60,008 for
Robin M. Silva, Reg. No. 38,304
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Customer Number: 67374
Morgan, Lewis & Bockius LLP
One Market, Spear Street Tower
San Francisco, CA 94105
Telephone: (415) 442-1000
Facsimile: (415) 442-1001